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Chapter 9

Kidney Diseases

Bones can break, muscles can atrophy, glands can loaf, even the brain can go to sleep, without immediately endangering our survival; but should the kidneys fail . . . neither bone, muscle, gland, nor brain could carry on.
Homer W. Smith (1895-1962)
From Fish to Philosopher, Ch. I

Introduction

Historical Perspective

For centuries, it has been known that dietary intake affects the composition of urine (see, for example, the discussion in the chapter on diabetes) and must, therefore, have an effect on kidney function. The idea that protein restriction might prevent further loss of kidney function in people with chronic renal insufficiency emerged during the first half of the 20th century (Addis 1948). Early studies in experimental animals suggested that excretion of urea by the kidney required "renal work." This idea received support from studies demonstrating that animals fed high-protein diets for prolonged time periods have enlarged kidneys as well as increased urea excretion. Early investigations also revealed significant increases in renal blood flow and glomerular filtration rates when meat was substituted for dietary carbohydrate or when extra protein was added to the diet (Brenner, Meyer, and Hostetter 1982).

These studies suggested that high-protein diets might stress the kidney workload to the point of failure. They also suggested that protein restriction might minimize the work required of kidneys that were already diseased and, thereby, prevent futher functional losses (Addis 1948). Additional research indicated that protein restriction could retard the progression of renal failure (Blatherwick and Medlar 1937; Farr and Smadel 1939; Addis 1948). However, the data supporting these observations were derived from rats, the study design was often faulty, and the applicability of these findings to humans—while of great interest—was uncertain.

In later decades, the development of kidney dialysis and transplantation techniques focused attention on methods—including manipulation of diet—to treat renal disease rather than to prevent it. Today, as more is learned about the progression of chronic renal disease, the role of diet in the etiology of this condition has become increasingly apparent.

Significance for Public Health

End-stage renal disease (ESRD) occurs when the kidneys are chronically unable to function sufficiently on their own, so that dialysis or kidney transplantation becomes necessary to maintain life. ESRD occurs in about 19,000 people each year in the United States (Schmidt, Blumenkrantz, and Wiegman 1983), and blacks are disproportionately affected as a result of hypertension-induced ESRD. Currently, about 80,000 persons undergo maintenance hemodialysis two or three times a week and another 11,000 persons undergo continuous ambulatory peritoneal dialysis (HCFA 1984). Approximately 9,000 kidney transplants were performed in 1986.

The estimated annual cost for maintenance hemodialysis and peritoneal dialysis treatment in the United States, including the expenses incurred by Medicare, State and private insurers, and Veterans Administration, military, and public health hospitals, is well over $2 billion (HCFA 1984). This estimate does not include the costs for pensions and from lost income, nor does it include the expenses for ancillary hospitalization, which is a frequent occurrence. A maintenance dialysis patient spends an average of approximately 15 to 16 days a year in the hospital (Blagg, Wahl, and Lamers 1983; Carlson et al. 1984). In addition to the financial costs of ESRD treatment, the patient and the patient's family often endure great physical and emotional suffering from the ravages of chronic renal failure, the frequent superimposed illnesses, and the burden of the treatment regimens.

Nutrition may affect persons who have, or are at risk for developing, ESRD in two ways. First, evidence shows that the intake of certain nutrients may influence the rate of progression of renal failure in persons with underlying renal disease. Second, individuals with advanced renal failure and those who undergo maintenance dialysis treatment often suffer from malnutrition and other nutritional disorders. It is possible, but not proved, that these nutrition-related complications may contribute to the debility, high incidence of superimposed illnesses, and poor rehabilitation typical of this condition.

Scientific Background

Functioning kidneys regulate the composition and volume of body fluids within very narrow limits. They do so by balancing intake and excretion of body fluids and the waste products derived from metabolic processes. If the kidneys fail to maintain homeostasis, a wide range of potentially lethal metabolic disorders can develop throughout the body.

Each human kidney contains about 1.2 million separate functional units called nephrons (Tisher and Madsen 1986), each with a glomerulus that removes ("clears") unwanted salts, waste products, and other chemicals from plasma along with the water in which they are dissolved. Normally, very little protein is removed. These substances are excreted from the kidney through a tubule that is connected to each glomerulus. The tubule can reabsorb back into the circulation most of the filtered water and some of the chemical substances, and it can actively remove other chemicals from blood. The fluids and chemicals that are not reabsorbed by the tubules drain into collecting ducts, flow through the ureter, and are stored in the bladder for eventual excretion as urine. The rate at which the glomeruli clear the blood of waste products is called the glomerular filtration rate (GFR).

Kidney Stones

When the concentration of certain salts in urine exceeds the limits of solubility, the salts can crystallize and form stones within the kidney or other parts of the urinary tract. The substances found most frequently in kidney stones include calcium, oxalate, phosphate, uric acid, and cystine (Smith, Van den Berg, and Wilson 1979). Although these substances derive from foods, oxalate and urate are also synthesized endogenously, and excessive dietary intake has not been shown to cause stone formation in healthy people. Instead, the supersaturated concentration of these substances in urine is the critical factor that set the stage for stone formation together with inadequate production of crystallization inhibitors (Kok, Papapoulos, and Bijvoet 1986) or inborn errors of metabolism that produce large amounts of the relevant metabolites.

Treatment of these conditions by diet or drugs is aimed at reducing the concentration of stone-forming substances in urine. The principal means to this end is to increase urine production to at least 2,500 ml per 24 hours by encouraging patients to drink water throughout the day unless on a low-fluid regimen (Smith, Van den Berg, and Wilson 1979).

Additional dietary measures to treat patients with chronic stone-forming conditions depend on the composition of the stones as well as on the genetic defect. For example, some persons who excrete excessive amounts of calcium in their urine reduce these levels in response to a low-calcium diet (Coe 1984); other persons increase calcium excretion, apparently because they compensate by synthesizing greater amounts of 1,25-dihydroxyvitamin D, absorbing more calcium, and increasing the release of calcium from bone (Broadus et al. 1984).

Dietary measures to reduce oxalate excretion include restriction of oxalate-rich foods, such as rhubarb, spinach, chocolate, and tea, and restriction of excessive intake of ascorbic acid (vitamin C), which is metabolized to oxalate. Uric acid stones have been treated with diets low in purine-rich foods, such as organ meats, fish, shellfish, and legumes. Persons with cystine-containing stones have responded successfully to low-protein diets (Sherrard 1983). Calcium phosphate stones have been treated successfully, if paradoxically, with high-phosphate diets that increase urinary excretion of pyrophosphate, an inhibitor of calcium crystallization (Smith, Van den Berg, and Wilson 1979). Reports that low-carbohydrate, low-protein, high-fiber, or vegetarian diets prevent stone formation have not been confirmed (Anonymous 1983).

Chronic Renal Failure

Chronic renal failure is permanent kidney damage with an associated depression of the GFR; it results in retention of waste products, abnormal plasma biochemistry, and symptoms ranging from lassitude to convulsions to death. Chronic renal failure is the consequence of longstanding and progressive renal damage and is usually irreversible. It may result from chronic glomerular disease (e.g., glomerulonephritis), chronic infections, polycystic kidneys or other congenital anomalies, vascular diseases, obstructive processes such as kidney stones, certain systemic or endocrine diseases, drug reactions, or hypertension.

The early stage of renal insufficiency occurs when the GFR falls to about 40 to 70 ml/min from a normal level of about 80 to 130 ml/min. Studies in animals with renal injury indicate that when the loss of kidney function causes renal insufficiency, the remaining functioning nephrons enlarge and the GFR increases (Deen et al. 1974; Hostetter et al. 1981). As a result of these adaptive changes, the loss of kidney function is proportionately less than might be expected from the loss of nephrons. In the injured or diseased kidney, increases in capillary blood flow and in the blood pressure gradient across the capillary wall have been reported (Hostetter, Troy, and Brenner

1981). Also, the chemical, electrical, and physical barriers to the movement of plasma proteins across the glomerulus into the renal tubule may be impaired (Olson et al. 1979, 1982).

For many years researchers have known that chronic renal disease often progresses to ESRD (Mitch et al. 1976; Rutherford et al. 1977; Adler and Kopple 1983; Klahr, Buerkert, and Purkerson 1983). Furthermore, the progressive loss of renal function occurs even in persons in whom the underlying cause of the renal disease has disappeared or abated—for example, in persons who have had relief of urinary tract obstruction, control of hypertension, or partial recovery from certain types of acute renal failure (McCormack et al. 1958; Kleinknecht et al. 1973; Rodriguez-Iturbe et al. 1976; Senekjian et al. 1979; Torres et al. 1980). Although the rate of progression of renal failure varies greatly among individuals, the decline in kidney function is constant in many individuals so that remaining function declines in approximately linear fashion (Mitch et al. 1976; Rutherford et al. 1977; Barsotti et al. 1981). It is not known in what percentage of persons with renal insufficiency will progress to renal failure, but the suspicion is that most people who lose more than 50 percent of their GFR will experience continued progression of the disease.

Chronic renal failure causes pervasive disorders in appetite as well as in the body's absorption, excretion, and metabolism of many nutrients. Consequently, nutritional therapy is essential in managing this condition. These disorders include: the accumulation in blood of urea and other waste products of protein metabolism and the clinical consequences of this accumulation (nausea, vomiting, and weakness leading to convulsions and coma) (Kopple 1978); a decreased ability of the kidney to either excrete a large salt load or to conserve salt when dietary sodium is restricted (Gonick et al. 1966); impaired ability to excrete water, potassium, magnesium, acids, and other compounds (David et al. 1972); a tendency to retain phosphorus (Bricker 1972; Coburn et al. 1977); decreased intestinal absorption of calcium (Coburn et al. 1977) and possibly iron (Lawson et al. 1971); and a high risk for developing certain vitamin deficiencies—particularly vitamin B_6, vitamin C, folic acid, and the active form of vitamin D, 1,25-dihydroxycholecalciferol, which is synthesized by the kidney (Kopple and Swendseid 1975).

The chronic renal failure patient is also likely to accumulate certain potentially toxic chemicals that normally are ingested in small amounts and excreted in the urine. Aluminum is such a toxin; it can cause severe bone disease, dementia, muscle weakness, and anemia in persons with kidney

failure (Elliott, MacDougall, and Fell 1978; Drueke 1980; Kaiser et al. 1984; Polinsky and Gruskin 1984). Currently, common sources of aluminum are the antacids aluminum hydroxide and aluminum carbonate, which persons with kidney disease frequently ingest to reduce intestinal absorption of phosphorus. Formerly, hemodialysis solutions contaminated with aluminum often caused aluminum toxicity, but such contamination has now been eliminated.

Acute Renal Failure

Acute renal failure is a general term used to describe a sudden decrease in the GFR, often to less than 2 percent of normal. Its early signs result from the accumulation of urea and other nitrogenous wastes. Electrolyte imbalance, metabolic acidosis, and other severe effects follow, as the person becomes increasingly uremic and other body systems are disrupted. Its most common causes are shock, severe infection, trauma, drugs, obstruction, and certain types of glomerulonephritis. In most instances, the condition is reversible if the person survives the underlying disease (Mitch and Wilmore 1988).

Despite the many advances in medical care during the past few decades, morbidity and mortality from acute renal failure remain high (Brezis, Rosen, and Epstein 1986). When associated with obstetrical complications, the mortality rate is about 17 percent; acute renal failure associated with surgery or trauma has a mortality of 51 to 53 percent (Brezis, Rosen, and Epstein 1986; Mitch and Wilmore 1988), and that caused by shock or sepsis accompanied by inadequate nutrition has a mortality rate of about 85 percent (Feinstein et al. 1981; Feinstein et al. 1983).

Protein-Energy Malnutrition in Renal Disease

One of the most prevalent nutritional complications of chronic renal failure is wasting, or protein-energy malnutrition (Kopple 1978, 1984). There are many causes for this wasting. Dietary intake, particularly of calories, is often inadequate (Kluthe et al. 1978; Kopple 1978; Salusky et al. 1983; Wolfson et al. 1984) because of loss of appetite due to the accumulation of toxins in kidney failure, the unappealing diets prescribed in renal failure, emotional depression, the debilitating effects of chronic illnesses, and the effects of acute superimposed illnesses on the patient's ability to eat or to accept intestinal tube feeding. The high incidence of superimposed illnesses can cause protein breakdown and wasting (Blagg, Wahl, and Lamers 1983; Carlson et al. 1984; Kopple 1984), as can the dialysis procedure itself. During dialysis, many biologically valuable nutrients may be lost (Kopple 1978), including amino acids, peptides, proteins (with peritoneal dialysis),

glucose (during hemodialysis with glucose-free dialysate), and certain water-soluble vitamins. The hemodialysis procedure also seems to increase net protein breakdown by unknown mechanisms (Borah et al. 1978; Farrell and Hone 1980). Renal failure patients sustain blood losses from frequent laboratory testing, occult gastrointestinal bleeding (very common in renal failure patients), and the sequestration of blood in the hemodialysis equipment (Linton et al. 1977). Because blood is rich in protein, these losses may cause serious protein depletion.

Patients with acute renal failure also demonstrate varying degrees of protein wasting. In some individuals, the net rate of protein breakdown (i.e., the difference between the total rate of protein degradation and protein synthesis in the body) may be very low—as little as 25 to 30 g/day, but in others, it may be as high as 240 g/day (Feinstein et al. 1981; Feinstein et al. 1983). For comparison, the total protein mass in a typical male is only about 6,000 g, excluding collagenous, or structural, fibrous protein (Cahill 1970). Patients with acute renal failure are often unwilling or unable to eat because of uremic poisoning or underlying illnesses such as abdominal infection, trauma, and surgical wounds. Thus, starvation often accompanies acute renal failure unless specific steps are inaugurated to nourish the patient.

In the United States, dialysis treatment is readily available for most patients with acute renal failure. Hence, patients with this condition do not often die from uremic poisoning; rather, death comes from complications such as infection associated with failure to heal wounds. Because, as discussed in the chapter on infections and immunity, protein-energy malnutrition may reduce the body's resistance to infection and impair wound healing, the profound wasting typical of acute renal failure may contribute to the high morbidity and mortality of this condition.

Dietary Management of Renal Failure

Diseased kidneys cannot clear metabolic waste products from the blood, maintain fluid and electrolyte balance, or convert vitamin D to its active form. The resulting elevated levels of nitrogenous wastes, electrolytes, and other metabolites can depress appetite and impair absorption of essential nutrients, thus establishing conditions that lead to uremia and malnutrition. Moreover, treatment of renal disease may demand severe dietary restrictions or induce nutrient losses. Dietary management of this condition, therefore, must provide protein, energy, and other essential nutrients in amounts adequate to avoid deficiencies but sufficiently restricted to avoid stressing the diminished excretory capacity of the diseased kidney. The goals of nutritional therapy for both acute and chronic renal failure are to

maintain optimal nutritional status, to minimize the toxic effects of excess urea in blood, to prevent loss of lean body mass, to promote patient well-being, to retard the progression of renal failure, and to postpone initiation of dialysis (Burton and Hirschman 1983; Abel 1983). In children, an additional goal is to maintain growth rates as close to normal as possible (Holliday 1983).

These goals are accomplished by the methods listed below.

Restricting Fluid Intake. Energy, protein, and other essential nutrients are provided in as small a fluid volume as is possible to maintain water balance.

Restricting Protein. Nitrogen balance must be maintained without any unnecessary accumulation of urea or other toxic nitrogenous waste products. The degree of protein restriction depends on the severity of renal damage as assessed by the use of GFR determinations. To enhance incorporation of amino acids into body protein and to reduce protein breakdown in more severely ill persons, dietary protein or supplements of high biologic value (containing a high proportion of essential amino acids) are often recommended (Burton and Hirschman 1983).

Increasing Energy Intake. The higher the energy intake, the less dietary protein is required to maintain nitrogen balance. Increasing the carbohydrate and fat content of the diet provides calories that do not stress the compromised excretory capacity of the kidney. This energy is protein-sparing; it improves nitrogen balance and prevents catabolism of body proteins. Patients with acute renal failure, however, are often unable to tolerate high carbohydrate loads and may require insulin administration (Abel 1983).

Regulating Phosphate, Calcium, and Magnesium Intake. Intake of certain nutrients must be monitored carefully to ensure that they do not accumulate in blood and cause problems. Phosphate restriction is necessary to prevent the metabolic bone disease that often accompanies renal failure; phosphate levels can also be regulated with phosphate-binding agents that cause dietary phosphate to be excreted rather than absorbed. Calcium may be administered as a supplement as needed. Excessive magnesium levels are not usually present unless magnesium-containing antacids are used; avoiding them or using magnesium-binding agents prevents toxic accumulation of this substance.

Supplementing Vitamins and Trace Elements. Supplemental water-soluble vitamins and trace elements are usually provided to compensate for inadequate intake and losses in dialysis.

Using Enteral and Parenteral Methods of Nutritional Support. Intravenous administration of nutrients and energy may be necessary for patients with acute renal failure who are unable to take food by mouth (Abel 1983). Administration of supplemental nutrients by mouth or tube has also proved helpful in certain cases.

Providing Appropriate Counseling and Support. Diets for renal patients are based on contradictory principles (meet nutritional needs but restrict protein and phosphorus), are especially restrictive, and require careful monitoring of the patient's nutritional status. Thus, trained nutrition professionals are usually essential for dietary management. Long-term nutrition counseling of patient and family is especially necessary for children with renal disease to promote growth without increasing the kidneys' excretory load (Holliday 1983).

Key Scientific Issues

- Role of Protein in Renal Disease
- Role of Phosphate in Renal Disease
- Role of Lipids in Renal Disease

Role of Protein in Renal Disease

Chronic Renal Failure

Renal function begins to decline in normal humans after about the fourth decade of life (Rowe et al. 1976), and it has been postulated that high-protein diets may contribute to this decline. Typical protein intake among Americans is considerably higher than the Recommended Dietary Allowance (RDA) for dietary protein (NRC 1980), and in healthy young men and women, a high protein intake has been noted to increase renal blood flow and the GFR (Pullman et al. 1954; Wiseman et al. 1987). There are also similarities between the type of scarring that occurs in normal aging human kidneys and the kidneys of rats fed high-protein diets. In adults who have had a congenital absence, failure of development, or surgical removal of one kidney during childhood, an abnormally high incidence of spontaneous

glomerular scarring occurs in the remaining kidney (Kiprov, Colvin, and McCluskey 1982). Although the precise cause is not known, one theory is that increased glomerular capillary blood flow and pressure associated with high-protein diets may contribute to progressive renal injury in certain individuals.

In rats, a high-protein diet stimulates an increase in glomerular filtration rate, capillary blood flow, capillary blood pressure gradients, and enlargement of individual nephrons, whereas a low-protein diet will blunt or prevent these responses (Hostetter et al. 1981). Normal rats fed high-protein diets throughout life have a higher incidence of renal disease in old age (Striker et al. 1969; Lalich, Faith, and Harding 1970; Everitt, Porter, and Wyndham 1982; Zucchelli et al. 1983). When fed a high-protein diet, rats with renal injury develop progressive renal failure. When such animals are fed a low-protein diet, the progression of renal failure is retarded or arrested (Blatherwick and Medlar 1937; Farr and Smadel 1939). One current hypothesis is that a high-protein intake causes filtration and excretion of protein and, thus, causes progressive injury to the glomerulus, including its basement membrane (filtering wall), by increasing both glomerular capillary blood flow and intracapillary blood pressure (Hostetter et al. 1981; Brenner, Meyer, and Hostetter 1982). This hypothesis further holds that a low-protein diet retards or stops progressive renal damage by preventing these high pressures and flow rates.

Traditionally, dietary protein restriction has been used to minimize the toxicity that occurs in renal failure (Kopple et al. 1968). Many of the waste products that accumulate in kidney failure are products of amino acid and protein metabolism. Current evidence suggests that some of these waste products cause toxic symptoms.

Recent studies in rats and humans have demonstrated that dietary control can retard the rate of progression of renal failure in a variety of renal diseases (Mitch et al. 1984). In rats, several models of renal insufficiency have been studied, including surgical removal of renal tissue, ligation of the arteries to the kidney, and experimental glomerulonephritis (Ibels et al. 1978; Karlinsky et al. 1980; Haut et al. 1980; Laouari et al. 1983; Kenner et al. 1985). In these animals, diets low in protein or phosphorus retarded or prevented progression of renal failure.

In humans with renal insufficiency, virtually all recent studies indicate that a diet low in protein or phosphorus retards the progression of renal failure (Maschio et al. 1982; Alvestrand, Ahlberg, and Bergstrom 1983; Barsotti et al. 1983; Barsotti et al. 1984; Gretz, Korb, and Strauch 1983; Mitch et al.

1984; Rosman et al. 1984). Each of these studies, however, has limitations inherent in experimental design related to the retrospective nature of many of the studies, an insufficient number of patients studied, the lack of control groups, poor documentation of patients' actual intake, and the paucity or absence of data that indicate whether these restrictive diets induce malnutrition. Adequate controls are especially important because not all persons with renal insufficiency progress to advanced renal failure, and the rate of progression can vary markedly from individual to individual.

In assessing protein restriction in renal failure management, some investigators have used a modified low-protein diet supplemented with the nine essential amino acids or with mixtures of some essential amino acids and ketoacid or hydroxyacid analogs of other essential amino acids (Walser 1975; Alvestrand, Ahlberg, and Bergstrom 1983; Barsotti et al. 1983; Gretz, Korb, and Strauch 1983; Mitch et al. 1984). The ketoacid or hydroxyacid analog is structurally identical to its corresponding essential amino acid, except that the amino group attached to the second (alpha) carbon of the amino acid is replaced with a keto group or hydroxy group, respectively (Figure 9-1).

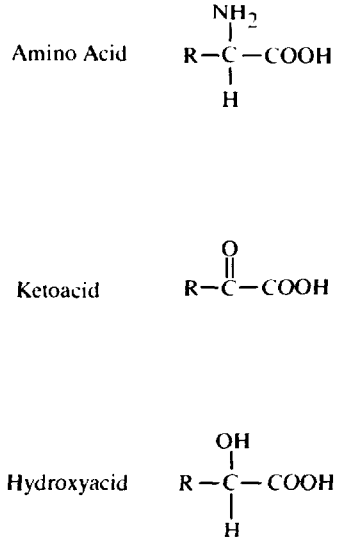

Figure 9-1. The comparative structures of amino acids, ketoacids, and hydroxyacids. The R symbol refers to the side chain of these chemicals, which is different for each individual compound.

Acute Renal Failure

Several studies in rats also indicate that a high amino acid intake by infusion may predispose to acute renal failure caused by loss of blood flow to the kidney (Zager and Venkatachalam 1983; Zager et al. 1983). The amino acid intake that predisposes to acute renal failure, when expressed per kilogram body weight, is not substantially greater than the quantity that might be consumed by humans. The reason for this effect is not known.

For unexplained reasons, acute renal failure causes a metabolic reorganization that promotes breakdown of muscle proteins and reduces the ability of the body to utilize amino acids to prevent wasting and to rebuild tissues (Clark and Mitch 1983). Although some studies in rats or humans support the benefits of nutritional therapy to prevent loss of body weight and protein mass in acute renal failure (Wilmore and Dudrick 1969; Toback 1977), most studies have not confirmed these observations. At the present time, no nutritional regimen prevents protein wasting in severely ill patients with this condition (Leonard, Luke, and Siegel 1975; Oken et al. 1980; Feinstein et al. 1981; Feinstein et al. 1983).

Merely increasing the protein intake does not stop acute wasting in many patients with acute renal failure (Feinstein et al. 1983). Giving large amounts of amino acids engenders formation of more urea with little or no evidence for increased accrual of body protein (Frohlich et al. 1974; Feinstein et al. 1981; Feinstein et al. 1983). Moreover, if greater quantities of nutrients are infused intravenously, an enhanced accumulation of water, minerals, and metabolic waste products may increase uremic poisoning or promote the need for more dialysis treatments. The inadequacies of current treatment methods for acute renal failure emphasize the importance of developing effective methods to prevent this condition.

Role of Phosphate in Renal Disease

Because the phosphate content of the diet is usually proportional to the protein content, it has been difficult to separate the effects of these nutrients on the progression of renal disease. Nevertheless, as mentioned above, diets low in phosphorus have been shown to retard the progression of renal failure in laboratory rats and in humans. One possible explanation is that a low phosphorus intake prevents the deposition of calcium phosphate in kidney tissue, which may cause further renal damage (Ibels et al. 1981; Alfrey and Tomford 1982). Whether low-phosphate diets prevent the onset of renal damage in humans has yet to be determined.

Role of Lipids in Renal Disease

Whether lipids and their metabolic products affect the development of progressive renal injury is still under investigation. Arachidonic acid is a fatty acid found in meat, fish, and certain plant foods; it is synthesized in the liver from linoleic acid and metabolized in the kidney into a family of eicosanoid compounds that include prostaglandins, thromboxanes, prostacyclins, leukotrienes (Dunn 1983). Prostaglandins affect blood flow and blood pressure inside the glomerulus, platelet aggregation, and the inflammatory process. Certain eicosanoids increase glomerular blood flow and pressure inside the glomerulus and may impair platelet clotting, while others have the opposite effect. In renal failure, there is an increased elaboration of certain eicosanoids in the kidney (Suzuki et al. 1980; Barcelli, Weiss, and Pollak 1982) that may delay further deterioration of kidney function (Klahr, Buerkert, and Purkerson 1983; Dunn 1983). The administration of prostaglandins also appears to affect the progression of chronic renal disease in animals (Zurier et al. 1977; Kelley, Winkelstein, and Izui 1979; McLeish et al. 1980).

Thus, reduced progression of renal injury and maintenance of a more normal GFR have been demonstrated in experiments in which rats and mice with impaired renal function were given fatty acid precursors of prostaglandins (Barcelli, Weiss, and Pollak 1982), injections of certain prostaglandins (Zurier et al. 1977; Kelley, Winkelstein, and Izui 1979), drugs that inhibit synthesis of prostaglandins that cause platelet clotting (Purkerson et al. 1985), or anticoagulants that inhibit platelet clotting (Purkerson et al. 1982).

These studies have been used to raise the hypothesis that renal disease may stimulate the glomerulus to synthesize eicosanoids that cause platelet clotting, inflammation, and replication of cells in the glomerulus, which, in turn, promote further renal injury (Purkerson et al. 1985). At the same time, inhibiting the synthesis of certain other eicosanoids in the glomerulus may protect the diseased kidney from continuing injury and from progressive loss of function. Because some eicosanoids appear to promote renal injury while others protect the diseased kidney from further damage, the dietary significance of these observations is as yet uncertain.

Implications for Public Health Policy

Dietary Guidance

General Public

Nutrients of particular interest in the occurrence of renal disease are protein, phosphate, and certain fatty acids. Although there is evidence in animals and humans that protein restriction can retard the progression of end-stage renal disease, there is no evidence that current protein intakes by the American population adversely affect the prevalence of renal disease.

Dietary phosphate restrictions have been noted to retard the progression of renal disease, but there is not sufficient evidence to indicate a role in the prevention of this condition. Nor may any implications be drawn for the general public on the relationship of dietary fatty acids intake to renal disease. Suggestions that certain lipids may increase the progression of renal disease have yielded conflicting research results.

Special Populations

Protein restriction is a therapeutic measure prescribed for patients with advanced renal disease, and end-stage renal disease patients on dialysis must follow a protein-, potassium-, and phosphate-restricted maintenance diet. A qualified health professional should provide information to such patients on using these diets appropriately.

Nutrition Programs and Services

Food Labels

Evidence related to the role of dietary factors in renal disease currently holds no special implications for change in policy related to food labeling.

Food Services

Evidence related to the role of dietary factors in renal disease currently holds no special implications for policy changes in food service programs.

Special Populations

Patients with renal disease should receive counseling and assistance in developing diets low in protein and low in phosphate. Those with renal stones should receive advice on diets that reduce excretion of stone-promoting factors (purines and excessive calcium) and should receive recommendations for a high daily fluid intake in excess of two liters.

Research and Surveillance

Research and surveillance issues of special priority related to the role of diet in renal disease should include investigations into:

- The ability of low-protein diets to retard the decline of renal function in normal aging.
- The mechanisms by which dietary protein affects renal function.
- The relationship of the role of dietary protein to that of phosphate in its effect on kidney function.
- The mechanisms by which other nutrients such as fatty acids or amino acids might affect renal function.
- The use of various diets—such as those low in protein or phosphate—to retard the rate of progression of renal failure.
- The relative merits of specialized formula diets, pharmacologic therapy, and traditional low-protein diets in treating progressive renal failure.
- The causes of wasting, malnutrition, and other nutritional disorders that occur in renal failure.
- The treatment—with calories, amino acids, or drugs—of wasting, malnutrition, and other nutritional disorders that occur in renal failure.
- The interplay of dietary factors (such as calcium, vitamin D, phosphate, protein, and oxalate) in the etiology of renal stones.
- The effect of omega-3 fatty acids in preventing the immune inflammatory response in chronic renal disease.
- The regulatory mechanisms in the utilization and metabolism of keto-acids in humans.
- The impact of reduced protein/amino acid intake on the quantitative dynamic status of protein and specific amino acid metabolism in organs and the entire body.
- Lipid metabolism as affected by reduced protein and amino acid intake.
- The role of lipids in the progression of chronic renal disease: lipid turnover by renal cells, effect on tubular growth and function, relationship of hyperlipidemia to renal injury, and effect of drugs in the treatment of hyperlipidemia.
- Control of renal growth and impact of nutrition on renal mass.

- Mechanisms that produce toxicity of uremia and consequences of uremic symptoms.
- Effect of protein restriction, as opposed to total calorie restriction, on renal injury.

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